

AMENDMENTS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method for inactivating hepatitis C virus (HCV) in a patient comprising administering to said patient a ~~modified~~ siRNA in an effective amount to inactivate said virus, wherein said ~~modified~~ siRNA ~~targets an HCV nucleotide sequence selected from the group consisting of~~ is at least 80% identical to 3' untranslated region (3' UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10 any one of SEQ ID NOS 1 and 10-28 ~~the sequence targeted by siRNA5.~~
2. (Currently Amended) The method of claim 1, wherein said ~~modified~~ siRNA is a ~~2' modified siRNA~~ further modified at the 2' position of at least one ribonucleotide.
3. (Canceled)
4. (Previously Presented) The method of claim 2, wherein said modification is selected from the group consisting of fluoro-, methyl-, methoxyethyl- and propyl-modification.
5. (Original) The method of claim 4, wherein said fluoro-modification is a 2'-fluoro-modification or a 2',2'-fluoro-modification.
6. (Currently Amended) The method of claim 5, wherein at least one pyrimidine of said siRNA is modified, ~~and said~~ wherein the at least one pyrimidine is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.
7. (Original) The method of claim 1, wherein both strands of said siRNA contain at least one modified nucleotide.
- 8-12. (Canceled)
13. (Currently Amended) The method of claim 1 ~~or 10~~, wherein said siRNA is siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.
14. (Currently Amended) A modified siRNA comprising at least one modified ribonucleotide, wherein said siRNA is resistant to RNase and retains the ability to inhibit

hepatitis C virus (HCV) replication, and wherein said modified siRNA ~~targets an HCV nucleotide sequence selected from the group consisting of~~ is at least 80% identical to 3'-~~untranslated region (3' UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10~~ any one of SEQ ID NOS 1 and 10-28 ~~the sequence targeted by siRNA5.~~

15. (Currently Amended) The modified siRNA of claim 14, wherein said modified siRNA is ~~a 2'-modified siRNA~~ modified at the 2' position of at least one ribonucleotide.

16. (Canceled)

17. (Previously Presented) The modified siRNA of claim 15, wherein the modification is selected from the group consisting of fluoro-, methyl-, methoxyethyl- and propyl-modification.

18. (Previously Presented) The modified siRNA of claim 17, wherein said fluoro-modification is a 2'-fluoro-modification or a 2',2'-fluoro-modification.

19. (Previously Presented) The modified siRNA of claim 18, wherein at least one pyrimidine of said siRNA is modified, ~~and said~~ wherein the at least one pyrimidine is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.

20. (Previously Presented) The modified siRNA of claim 14, wherein both strands of the siRNA contain at least one modified nucleotides.

21-23. (Canceled)

24. (Currently Amended) A method of making a modified siRNA that targets a nucleic acid sequence in hepatitis C virus (HCV) comprising:

(a) preparing a modified-double stranded RNA (dsRNA) fragment containing at least one modified ribonucleotide at least 80% identical to any one of SEQ ID NOS 1 and 10-28 ~~in at least one strand that spans 3' untranslated region (3' UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, or the sequence targeted by siRNA5;~~ and

(b) cleaving said modified-dsRNA fragment with Dicer resulting in at least one modified siRNA ~~that targets an HCV nucleotide sequence selected from the group consisting of 3' untranslated region (3' UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10, and the sequence targeted by siRNA5~~ capable of inactivating said virus.

25. (Previously Presented) The method of claim 24, further comprising:

(c) isolating said at least one modified siRNA.

26-42. (Canceled)

43. (Currently amended) A double-stranded RNA molecule ~~of from about 10 to about 30 nucleotides that inhibits replication of hepatitis C virus (HCV) and targets an HCV nucleotide sequence selected from the group consisting of~~ is at least 80% identical to 3' untranslated region (3' UTR), NS3 helicase, C1, C2, C3, C4, C5, 5B1, 5B2, 5B3, 5B4, 5B5, 5B6, 5B7, 5B8, 5U8, 5U9, 5U10 ~~any one of SEQ ID NOS 1 and 10-28 the sequence targeted by~~ siRNA5.

44. (Currently Amended) The double-stranded RNA molecule of claim 43 ~~comprising a nucleotide sequence~~ at least 80% identical to the nucleotide sequence of siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.

45. (Currently Amended) A method of inducing targeted RNA interference toward HCV in hepatic cells, comprising administering the double-stranded RNA molecule of claim 43 to hepatic cells, ~~wherein the nucleotide sequence of said double-stranded RNA molecule corresponds to the targeted HCV nucleotide sequence.~~

46. (Currently Amended) A method of inhibiting replication of hepatitis C virus (HCV), comprising administering the double-stranded RNA ~~polynucleotide~~ molecule of claim ~~[[44]]~~ 43 to cells infected with HCV.

47. (Original) A vector comprising a DNA segment encoding the RNA molecule of claim 43.

48. (Previously Presented) The vector of claim 47, wherein the sense strand of said double-stranded RNA molecule is operably linked to a first promoter and wherein the antisense strand of said double-stranded RNA molecule is operably linked to a second promoter.
49. (Original) The vector of claim 48, wherein said first and second promoters are selected from the group consisting of U6 and H1.
50. (Original) The vector of claim 48 wherein said first and second promoters are the same.
51. (Original) The vector of claim 47, wherein the sense and antisense strands of said RNA molecule are under the control of a single promoter.
52. (Original) The vector of claim 51, wherein said single promoter is selected from the group consisting of U6 and H1.
53. (Original) A host cell comprising the vector of claim 47.
54. (Original) A method of inhibiting replication of hepatitis C virus (HCV) in cells carrying HCV, comprising transfecting said cells with the vector of claim 47.
55. (Currently Amended) A method of treating hepatitis C infection in a subject in need thereof, comprising administering a composition comprising a therapeutically effective amount of the double-stranded RNA molecule of claim 43 to said subject.
56. (Currently Amended) A method of treating hepatitis C infection in a subject in need thereof, comprising administering the vector of claim 47 to said subject.
- 57-66. (Canceled)
67. (Currently Amended) The method of claim 1, wherein said ~~modified~~ siRNA is further modified in at least one nucleotide base.

68. (Currently Amended) The method of claim 67, wherein the at least one nucleotide base is a pyrimidine ~~of said siRNA is modified~~, and said ~~at least one~~ pyrimidine is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.

69. (Currently Amended) The method of claim 1, wherein said ~~modified~~ siRNA is further modified in at least one phosphate linkage.

70. (Previously Presented) The modified siRNA of claim 14, wherein said modified siRNA is modified in at least one nucleotide base.

71. (Currently Amended) The modified siRNA of claim 70, wherein the at least one nucleotide base is a pyrimidine ~~of said siRNA is modified~~, and said ~~at least one~~ pyrimidine is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.

72. (Previously Presented) The modified siRNA of claim 14, wherein said modified siRNA is modified in at least one phosphate linkage.

73. (Previously Presented) The method of claim 28, wherein said modified siRNA is modified in at least one nucleotide base.

74. (Currently Amended) The modified siRNA of claim 73, wherein the at least one nucleotide base is a pyrimidine ~~of said siRNA is modified~~, and said ~~at least one~~ pyrimidine is cytosine, a derivative of cytosine, uracil, a derivative of uracil or a combination thereof.

75-80. (Canceled)

81. (Previously Presented) The modified siRNA of claim 14 comprising a nucleotide sequence at least 80% identical to the nucleotide sequence of siRNA5, siRNAC1, siRNAC2, siRNA5B1, siRNA5B2 or siRNA5B4.

82. (New) The method of claim 1, wherein said siRNA is at least 90% identical to any one of SEQ ID NOS 1 and 10-28.

83. (New) The method of claim 1, wherein said siRNA is at least 95% identical to any one of SEQ ID NOS 1 and 10-28.

84. (New) The method of claim 1, wherein said siRNA is at least 97% identical to any one of SEQ ID NOS 1 and 10-28.

85. (New) The method of claim 14, wherein said modified siRNA is at least 90% identical to any one of SEQ ID NOS 1 and 10-28.

86. (New) The method of claim 14, wherein said modified siRNA is at least 95% identical to any one of SEQ ID NOS 1 and 10-28.

87. (New) The method of claim 14, wherein said modified siRNA is at least 97% identical to any one of SEQ ID NOS 1 and 10-28.

88. (New) The method of claim 43, wherein said siRNA is at least 95% identical to any one of SEQ ID NOS 1 and 10-28.

89. (New) The method of claim 43, wherein said siRNA is at least 97% identical to any one of SEQ ID NOS 1 and 10-28.

90. (New) The method of claim 43, wherein said siRNA is at least 98% identical to any one of SEQ ID NOS 1 and 10-28.

91. (New) The method of claim 43, wherein said siRNA is at least 99% identical to any one of SEQ ID NOS 1 and 10-28.